Renal Cell Cancer: Bench Surgery and Autotransplantation for Complex Localised Disease

Gerald H.J. Mickisch*
Center of Operative Urology Bremen, Academic Hospital Bremen “Links der Weser”, Bremen, Germany

Abstract

Objective: The strongly increased availability of haemodialysis has limited the number of bench surgeries followed by autotransplantation for complex cases of renal cell carcinoma (RCC) in solitary kidneys during the 1980s and 1990s. However, during recent years, quality-of-life issues, cost aspects, and the relatively high attrition rate under long-term haemodialysis have sparked renewed interest in organ-preserving bench surgery strongly driven by patients’ demands.

Methods: We reviewed our experience with 36 recent cases of bench surgery and autotransplantation for complex RCC collected prospectively in our database.

Results: All tumours were invariably RCCs. In 32 cases a clear-cell type, in 3 cases a papillary type, and in one case a chromophobe type of carcinoma was diagnosed. All cases were considered preoperatively by imaging procedures as “organ-confined,” whereas definitive pathology revealed a tumour stage ranging from pT1 to pT3a, always pN0, and M0. Surgical complications were few, but significant: one perioperative death after 5 d due to myocardial infarction, one kidney lost due to transplantation failure, and one patient on haemodialysis for 3 wk until complete functional recovery. Oncologically, after a relatively short follow-up period of 2.8 yr (median), one patient had distant metastasis and one patient had a recurrent tumour in his kidney after 13 mo.

Conclusion: When critically appraising our personal experience consisting of 21 retrospective cases from 1992 to 2000 and of 36 prospective cases (this series) from 2001 to 2006, bench surgery and autotransplantation for complex cases of RCC are feasible and probably cost effective. There is a clear need for strict inclusion criteria such as an imperative indication and organ-confined (hence, surgically curable disease) stages, a multidisciplinary team approach, suitable infrastructure, and experience in major surgical procedures. If these criteria are met, bench surgery followed by autotransplantation has become again a valuable last resort and is apparently safe.

* Center of Operative Urology Bremen, Academic Hospital Bremen Links der Weser, Robert-Koch-Str. 34a, D-28277 Bremen, Germany. Tel. +49 421 8700 300; Fax: +49 421 8700 309. E-mail address: gerald.mickisch@coub.de.

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1. Introduction and objective

Approximately 2–3% of all malignant tumours in adults develop in the kidney. In 85% of them, the tumour originates from cells of the proximal tubules and is known as Grawitz tumour, a hypernephroma or a renal cell carcinoma (RCC). In The Netherlands, the annual incidence of the third most common urologic tumour is about 11/100,000. Men are twice as often afflicted as women, most often in the fifth to sixth decade. At the time of diagnosis, about 20% of the patients have disseminated disease and another 25% will have locally advanced disease. The incidence of RCC has gradually increased over the years and, based on results in contemporary series, approximately 40% of all patients with this disease will die of it.

Traditionally, the classic presentation of a patient with kidney carcinoma consisted of a flank pain, macroscopic haematuria, and a palpable abdominal mass. Nowadays, more than half of all tumours are incidental findings during the investigation of other symptoms, such as high blood pressure, low-grade pyrexia, weight loss, and increased erythrocyte sedimentation rate [1]. Another 25% are diagnosed during routine ultrasound examinations. Undoubtedly, with the increasing availability of ultrasonography or computed tomography (CT) scanning, incidental renal tumours are more frequently diagnosed. Therefore, the cohort of patients that seeks treatment for RCC has dramatically changed over the last 25 yr, and the question arises whether this alteration should also translate into different approaches to surgical treatment strategies.

An organ-sparing resection, sometimes called "partial nephrectomy" of a malignant tumour is the most flagrant violation of Robson’s concepts of a “radical” tumour nephrectomy [2]. Here, the surgeon deliberately opens Gerota’s fascia, frees the kidney from surrounding fatty tissue, and resects the tumour only. The techniques applied in various series [3] ranged from tumour excision over truly “partial” nephrectomy to ex vivo (bench) surgery. Nevertheless, from a theoretical viewpoint, the tumour dissection must be performed within a safe rim of healthy parenchyma guided by intraoperative frozen section analysis to avoid margin positivity responsible for local recurrence.

Indications for nephron-sparing surgery evolved out of necessity when malignancy was detected in a solitary kidney or in the setting of bilateral cancer or diminished renal function. Results were reasonable with a mean recurrence rate of 7.5% [4]. More recently, in a review article about a single-centre study with 500 patients [5] preservation of kidney function was achieved in 489 patients (98%), exhibiting a cancer-specific 5-yr survival rate of 93%. Recurrent RCC developed postoperatively in 39 of 473 patients (8.2%); 13 of these patients (2.7%) were diagnosed with a local recurrence in the remnant kidney, whereas 26 developed metastatic disease.

Local recurrence was reported in 3 cases in a review article [4] incorporating 388 cases of elective nephron-sparing operations from 11 centres, which comprised local recurrences in 2 cases and metachronous recurrence elsewhere in the kidney in a single case. At a mean follow-up of 31–75 mo, the local recurrence rate was 0.8%, which is 10 times lower than after a mandatory indication for kidney-sparing operations. Suffice it to say that appropriate patient selection is partly responsible for this excellent outcome. There is consensus that, in addition to the size of the primary tumour, the feasibility of a radical resection in terms of the anatomic localisation of the cancerous mass is critical [6]. In most series, elective indications are reserved for tumours ≤4 cm in diameter.

In some few cases of a solitary kidney and an organ-confined albeit extensive or centrally located RCC, organ-sparing approaches are warranted, but technically not feasible in situ for a safe tumour resection without compromising remaining kidney function. In those exceptional cases, bench surgery followed by autotransplantation may be indicated. This surgically challenging procedure should be regarded as the last resort and may render acceptable results when strict selection criteria, multidisciplinary team work structures, and adequate quality control measures are applied. These conditions are best met in the context of “A Centre of Excellence” using defined protocols for inclusion and therapeutic outcome measurements. This is the topic of the present paper.

2. Materials and methods

We report here on a prospective series of 36 cases of bench surgery followed by autotransplantation for complex RCC. The surgical procedure was performed by a multidisciplinary team consisting of a nephrologist specialising in hemodialysis, a transplant surgeon familiar with kidney transplantation procedures, and a urologic surgeon specialising in oncologic urology, who served as a team leader (G.H.J.M.). All patients were unanimously attested by the whole team to have an imperative indication for this operation and were considered to be suitable surgical candidates. Informed consent was obtained after discussing possible alternative strategies such as a tumour nephrectomy followed by haemodialysis and kidney transplantation in the follow-up period. Institutional
ethical committees were duly informed of our treatment protocol and approved enrolment, treatment, and follow-up criteria.

These criteria were established in 2000 when we retrospectively analysed our preceding series of 21 cases of bench surgery and autotransplantation that were operated by us at the Department of Urology, Erasmus Medical Center, Rotterdam, The Netherlands from 1992 to 2000 among 244 organ-sparing kidney tumour excisions (8.2%).

3. Results

Our series consists of two parts. The first part comprised 16 successful cases of bench surgery with autotransplantation and two aborted attempts. These operations were performed at the Erasmus Medical Center, Rotterdam, The Netherlands, from January 2001 until August 2002. Thereafter, the project leader (G.H.J.M.) changed institutions. The second part included 20 patients who were operated on from November 2002 until September 2006 by Dr. Mickisch at various institutions with a majority in Bremen, Germany, at the Center of Operative Urology (COUB) using the same inclusion criteria and same surgical strategies as in the first part of this series.

All tumours were invariably RCCs. In 32 cases a clear-cell type, in 3 cases a papillary type, and in one case a chromophobe type of carcinoma was diagnosed at histopathologic examination. All cases were considered preoperatively by imaging procedures as “organ-confined” (Figs. 1 and 2), whereas definitive pathology revealed a tumour stage ranging from pT1 to pT3a, always pN0, and M0 (Union Internationale Contre le Cancer [UICC] classification, 2002 edition; Figs. 3 and 4). In two patients (see above), we did not carry out the autotransplantation.

In one patient we detected an unsuspected tumour-positive lymph node at frozen section analysis, and in the other, one of three resected tumours was a Bellini duct type of carcinoma. Because of the highly aggressive nature of this tumour entity, we did not dare to retransplant the kidney.

The reason for this kind of complex surgery was always an imperative indication, namely, 33 solitary kidneys (27 large central masses and 8 bilateral tumours). In one patient with multiple bilateral tumours, a tumour nephrectomy on one side, and bench surgery with autotransplantation on the other side, were performed in two sessions. Patient were aged 31–70 yr with a median age of 48 yr. Preoperative creatinine levels varied from 59 to 221 uM (median, 99 uM; normal range < 150 uM).

Surgical techniques followed generally the principles of a Robson [2] type of radical nephrectomy using a modified Giuliani (anterior flank) incision.

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Fig. 1 – Imaging procedures: magnetic resonance imaging (case 1).

Fig. 2 – Imaging procedures: computed tomography angiography (case 2).

Fig. 3 – Radical tumour resection (case 1).
In cases with an absent/dysfunctional contra-
lateral adrenal gland, the ipsilateral adrenal gland
was preserved in the case of undetectable tumour
invasion. In addition, some kidney transplantation
features were included such as resecting long vas-
cular sleeves and using heparin as well as inducing
osmotic diuresis by mannitol prior to clamping the
renal artery. The resected kidney was placed imme-
diately on crushed ice (sterile working bench) and
flushed with EURO-Collins solution at 4 °C. The
kidney specimen was freed from all adjacent fatty
tissues, and the tumour was resected radically using
magnifying glasses or a surgical microscope. Multiple
frozen sections were analysed to ensure radicality.
Following renal reconstruction, an autotransplanta-
tion to the fossa iliaca was performed. Ureteric
anastomosis was done either by formal antirefluxive
implantation to the bladder or by ureteroureteros-
tomy to the remnant ureteric stump.

Overall, surgical time (from incision to final
wound closure) ranged from 320 to 560 min (median,
370 min), and total blood loss as calculated from
anaesthesiology charts varied from 170 to 620 ml
with a median of 310 ml. Postoperative serum
creatinine levels ranged from 71 to 239 uM (median,
144 uM; normal range < 150 uM).

Surgical complications were few, but significant:
one perioperative death after 5 d due to myocardial
infarction, one kidney lost due to transplantation
failure, and one patient on hemodialysis for 3 wk
until complete functional recovery.

Oncologically, we noted, after a relatively short
follow-up period of 2.8 yr (median), one patient with
distant metastasis and one patient with a recurrent
tumour in his kidney after 13 mo, which may have
been a true local recurrence or a secondary tumour.

This situation was salvaged by nephrectomy of the
autotransplant.

4. Discussion

The first successful kidney transplantation was
performed on 23 December 1954, and the surgical
pioneer, Dr. M.E. Murray received the Nobel Prize
in 1990. Identical twins to circumvent inherent
immunologic problems were the first patients to
benefit from this revolutionary progress in surgical
medicine, and graft survival extended to 11 mo. Currently, a 60–80% 5-yr allogeneic graft survival is
standard practice for kidney transplantation in
Europe.

In the 1960s, the medical community experienced
increasing numbers of bench surgery with kidney
autotransplantations, which were often done for
chronic benign diseases (chronic kidney failure) and
some few RCCs. In the 1970, peak incidences of this
type of complex surgery were described, and RCC
became an established indication [8]. The 1980s
were characterised by decreasing numbers of this
technique, parallel to the increasing availability of
hemodialysis [9], and in the 1990s, only a few case
reports appeared advocating this surgical challenge
[10,11].

Nevertheless, in the last couple of years, there
has been a remarkable revival in interest in bench
surgery followed by autotransplantation. Several
reasons may have contributed to this development:
First and probably most important, there is a critical
shortage of kidney donations suitable for transplan-
tation, and patients with tumours are not a priority
for transplant centres. Hence, the alternative strat-
 egy for complex RCC to simply nephrectomise the
patient and transplant a donor kidney at a later stage
while bridging the waiting period by hemodialysis
has been seriously hampered by long and cumber-
some waiting lists. Second, hemodialysis has proven
to reduce quality of life significantly, carries mor-
bidity and mortality, and is expensive.

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![Fig. 4 - Tumour resection: organ-confined, albeit extensive
disease (case 2).](image-url)
last resort and is apparently safe, and requests are steadily increasing.

Acknowledgements

In the first part of this series (Rotterdam cases), the transplantation surgeon J. IJzermans, MD, and the nephrologist M. Fieren, MD, contributed significantly to our multidisciplinary team approach. In addition, the urologic surgeons, W. Kirkels, MD, and P. Verhagen, MD, contributed some cases.

References